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September, 1949

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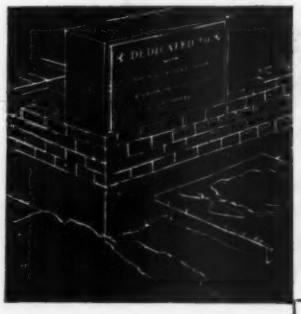

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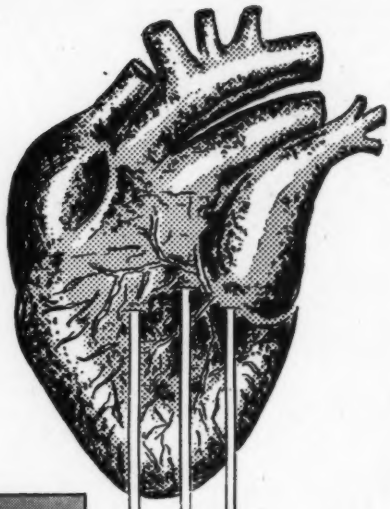

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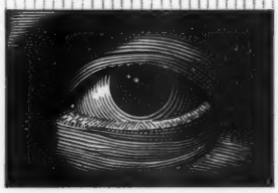

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1. Mayer, L. L.: Arch. Ophth. 39:232, 1948.
2. Thygeson, P., in discussion on Mayer, L. L.: Arch. Ophth. 39:232, 1948.

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A NECESSARY RESEARCH PROBLEM

The controversy existing as to the proper therapy for treatment of venous thrombosis still goes on. Very recently Dr. Alton Ochsner made the statement, in discussing this problem, that in New Orleans they were attempting to approach this problem on a middle ground, using both anti-coagulant therapy and surgical ligation. This, of course, is as it should be. There can be no doubt that there has existed a great deal of dogmatism as regards this subject; and perhaps the treatment of venous thrombosis has been overemphasized.

The real treatment of venous thrombosis is its prevention. While it is fully understood that progress has been made as regards prophylaxis, such as various types of exercise, early ambulation, etc., we are still at a loss to decide which patient will develop venous thrombosis, and which patient will not. Various research projects have been instituted to study the prophylaxis, but our progress to date has not been exceptional.

Attempts have been made to study the degree that the platelets develop adhesive power. This co-efficient can not be accurately determined. The patient's tolerance to heparin has been studied, and the heparin tolerance test is used in some of the clinics. However, there is still some question as to its accuracy. We must, and shall, continue our research in this direction.

There are available for clinical use two anti-coagulants, heparin and dicumarol. Neither of these are perfect; and, while their use is more or less universal, they are not what one might call popular therapeutic agents. What we must have is a safer anticoagulant. By the term, safer, one predicates an anti-coagulant that the patient may take similarly, let us say, as he takes insulin.

Some test must be devised that the patient can do each morning in his home, the same as a diabetic tests his own urine. This test must accurately and easily determine the coagulating power of the blood. It must have a universal technique, and a universal interpretation. The safe anti-coagulant must have a non-toxic an-

tidote which the patient may take himself, and not require extensive laboratory procedure before and after its use.

Our present anti-coagulants have a very definite place in the practice of medicine today. They are a distinct advance. They are, and should be used; but the difficulty in administration of heparin and the laboratory control required in dicumarol therapy mitigates the universal use which they should have, at least as a prophylactic measure.

In large institutions where this type of therapy is being employed daily, it is entirely feasible to have what might be called an anti-coagulant team that supervises this therapy throughout the whole institution.

This is fine, but how about the practitioner in our section of the country, whose patients are often great distances apart? His difficulty in handling this type of therapy is readily appreciated by all of us. Research must provide us with a more adequate anti-coagulant substance.

Research on this controversial subject must be accelerated. It is granted that in the past 15 years a great deal of progress has been made, but the progress, while great, is not wholly adequate. We must determine which patients have a predilection for venous thrombosis, and we must devise a more adequate drug for use in anti-coagulant therapy. Until we do this, we will not have solved this problem, because the problem can only be solved by prophylaxis.

Thrombosis And Embolism

Although a great deal has been written on the subject of thrombophlebitis, bland thrombosis or phlebothrombosis, and pulmonary embolism in the past few years, there is still need for organizing the facts available and for constant vigilance in watching for the physical signs that **usually** appear when thrombosis or pulmonary embolism occur. Trauma, either surgical or from external injury, cardiac impairment, cancer, inadequate correction of blood or nutritional disorders as preparation for surgery, and advancing years, are all predisposing factors to be borne in mind. Prophylactic measures, such as bed exercises, early ambulation, proper preparation for surgery, and avoidance of trauma to tissues and vessels during surgery are all important. Anticoagulant therapy preoperatively is advocated by some for the type of patient who seems especially liable to incur a thrombus, but as yet there is no general acceptance of such a procedure.

Zimmerman [1] and his associates at Michael Reese Hospital in Chicago, surveyed the clinical and pathological records of 9,980 patients who died over a period of 16 years, with reference to pulmonary embolism and antecedent vein disease. Autopsy records were available for 5,588, or 56 per cent of these. Pulmonary emboli were divided into three classes:

(1) The largest group, small emboli which were entirely incidental and obviously played no part in causing death. These usually occurred in patients with heart disease, pneumonia, cancer or other diseases.

(2) Larger emboli, with infarctions, where it was felt that the emboli might have contributed to the patient's death;

(3) Fatal emboli, where death was due directly to the embolus.

Three hundred and forty-five cases of pulmonary embolism were found, 166 of which were listed as purely incidental, 123 as contributory, and 56 as large, fatal emboli, an incidence of 1.0 per cent of all the autopsies. Fifty-three of the 56 fatal emboli came from bland thrombi and three from areas of thrombophlebitis. This bears out the accepted fact that the bland thrombus or phlebothrombosis, is the unattached, dangerous thrombus, while in thrombophlebitis the thrombus is firmly attached to the vein wall and has little tendency to loosen. However, a soft, red thrombus may develop in an inflamed vein and occasionally break off.

This is what occurred in the three cases of thrombophlebitis. The incidental emboli usually came from the heart and occurred most frequently in medical cases, whereas the fatal ones almost always had their source in the large veins of the lower extremities and were found chiefly in surgical cases. Forty-three fatal emboli were found in patients who had undergone major surgery, in a total number of 152,371 major operations. Based on the autopsy per centage of 56, it could thus be estimated that embolism was the primary cause of death in 0.05 per cent of patients undergoing major surgery, or an incidence of one in 2,000. From this estimate it would appear that fatal pulmonary emboli are much less common than recent statistics would have us believe.

Nevertheless, there should be no slackening of vigilance in looking for signs of vein diseases, or in prophylactic efforts, or in treatment once the presence of thrombosis or thrombophlebitis is established. These symptoms and signs are well known, but to arrange them in their order of frequency is instructive. Felder [2] studied 92 cases representing venous disease in 105 extremities and found them to occur as follows:

(1) Swelling of the extremity occurred in 88.5 per cent, but was sometimes only discernible by measurement of the calf.

(2) Tenderness in the calf muscles, especially to deep pressure, was next most frequent, appearing in 75 per cent.

(3) Heat—53 per cent.

(4) Pain or tightness of the calf or thigh muscles when at rest, 53 per cent.

(5) Homans' sign (pain in the calf on passive dorsiflexion of the foot) 49.5 per cent. Color changes or dilated superficial veins were found infrequently.

Treatment of the patient with a thrombosed extremity has been a highly controversial subject, but with the better knowledge of pathologic processes, the advent of the anticoagulant agents dicumarol and heparin, and the prompt ligation of the common femoral vein when this is necessary, morbidity and mortality from this disease should become steadily less. At present the judicious use of chemotherapy, antibiotics and the anticoagulants) where adequate laboratory control is available) are indicated for acute thrombophlebitis, while in phlebothrombosis, often asymptomatic, ligation of the common femoral vein at the level of the superfician femoral, is

required. Some recommend bilateral ligation, but this too is still a matter of controversy.—By E. A. RYGH, M.D., Santa Rita, N. M., Hospital.

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1—Zimmerman, Leo M., M.D., Miller, Daniel, M.D., and Marshall, Alfred N., M.D.—Surgery, Gynecology and Obstetrics—1949, 88:373-388.

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Southwestern Medical Conference Nov. 9-12 In Albuquerque, N. M.

Plans are developing nicely for the annual conference of the Southwestern Medical Association, which will be combined this year with the meeting of the New Mexico Division of the American Cancer Society in the Hilton Hotel in Albuquerque, Nov. 9, 10, 11 and 12.

Members and other physicians who expect to attend are urged to make reservations well in advance by writing to:

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Among the impressive list of speakers on a wide variety of timely scientific subjects will be:

(1) **E. W. Pernokis, M.D.,** Associate Professor of Medicine, University of Illinois—Anemias and Leukemia.

(2) **Elmer Belt, M.D.,** Director of Belt Urologic Group, Los Angeles, California—Ureteral Intestinal Anastomosis; Urology for the General Practitioner.

(3) **Herbert Willy Meyer, M.B.,** Professor of Clinical Surgery, Post-Graduate Medical School, New York University—Cancer of the Breast; Diaphragmatic Hernia; Perforation of the G-I Tract.

(4) **Donald M. Pillsbury, M.D.,** Professor of Dermatology and Syphilology, University of Pennsylvania—Malignant Skin Lesions; Dermatology As Applied to the General Practitioner.

(5) **Allan Butler, M.D.,** Associate Professor of Pediatrics, Harvard University—Malignancies in Childhood; Fever of Undetermined Origin.

(6) **Herbert F. Traut, M.D.,** Professor of Obstetrics and Gynecology, University of California Medical School—Use of Vaginal Smear in General Gynecologic Diagnosis; Bleeding in the Third Stage of Labor.

(7) **Otto C. Brantigan, M.D.,** Professor of Clinical Surgery and Surgical Anatomy, University of Maryland, Chief of Thoracentesis Surgery, University of Baltimore; Chief Surgeon, Baltimore City Hospital—Carcinoma of Lung; Surgical Treatment of Peptic Ulcers.

(8) **E. T. Bell, M.D.,** Professor of Pathology, University of Minnesota—Experimental Production of Carcinoma.

(9) **William Rettberg,** Associate Professor of Medicine, University of Colorado School of Medicine—Present Status of Antibiotics.

(10) **William Boyd,** Professor of Pathology, University of Toronto, Canada—Subject to be announced.

Upon completion of plans, further announcements will be given.

—By H. J. BECK, M.D., Albuquerque, Secretary Southwestern Medical Association Conference.

Dr. J. Richard Fuchlow

Dr. J. Richard Fuchlow, 45, El Paso radiologist who died suddenly in his home on the night of July 21, will be greatly missed by his fellow physicians of the Southwest.

DR. FUCHLOW

Dr. Fuchlow won the affection of both patients and members of the profession for the intense and sympathetic interest he took in each case with which he was associated. He was particularly active in work of the El Paso County Medical Society's Tumor Clinic, the El Paso Tuberculosis Association and William Beaumont General Hospital.

As head of the Society's committee in charge of the Tumor Clinic, he was in regular attendance at the Clinic's weekly meetings, where any doctor can bring a case for discussion of diagnosis and proper treatment. He worked diligently to make the Clinic's X-Ray filing system as complete as possible. Frequently he presented to the Clinic unusual cases from William Beaumont General Hospital, where he was a consultant. He was always interested in bringing physicians of national importance to speak before the Clinic and County Medical Society meetings. On many occasions he spoke over the radio in the drive for funds to fight cancer.

Glenn E. Camp, president of the El Paso Tuberculosis Association, of which Dr. Fuchlow was third vice-president, wrote, "The Association suffered an irreplaceable loss with the sudden death of Dr. Fuchlow. He worked tirelessly and without thought of compensation in helping us carry on our extensive X-Ray program, but more valuable still were his friendship and optimism and his wise counsel on the many problems that faced us."

A native of Pennsylvania, Dr. Fuchlow received his Bachelor of Medicine and Bachelor of Science degrees at St. Thomas College in St. Paul, Minn., and his Doctorate in Medicine at the University of Minnesota. He served for three years in the Army Medical Corps at Fort Riley, Kan., and then did graduate work at Ventura, Calif., and Memphis, Tenn. For five years he practiced medicine in Rapid City, S. D., where he was in charge of radiology at the Sisters of St. John's Hospital and the General Hospital. He was also in charge of radiology in the Sisters' Hospital in Deadwood, S. D., during this period.

Dr. Fuchlow came to El Paso in 1944. He was a member of the Radiological Society of North America, the American College of Radiology, the Rocky Mountain Radiological Society, the State Medical Association of Texas, and a member of the consulting staff at Hotel Dieu in El Paso.

He is survived by his widow; a daughter, Anne, and two sons, Richard and William, all of El Paso.

VENOUS THROMBOSIS AND PULMONARY EMBOLISM, THE CAUSES, PREVENTION AND TREATMENT

ROBERT R. LINTON, M.D.
Boston, Massachusetts

(From the Depts. of Surgery of the Massachusetts General Hospital and the Harvard Medical School)

The subject of thromboembolism is of interest to all practicing physicians and surgeons, but one which creates today more controversy than almost any other in the field of medicine and surgery. There are two schools of thought in regard to the treatment of this disease, but it is not my intention to convince you of either one or the other. I merely wish to present the facts as we have gathered them at the Massachusetts General Hospital over the past ten or more years.

Irrespective of what branch of medicine or surgery one is in, we have all witnessed the sudden demise of a patient from a massive pulmonary embolus, who was making apparently a very satisfactory convalescence either from a surgical operation, a normal pregnancy, a fracture of the leg, or trauma to an extremity. It is this condition which we are primarily interested in preventing, since so many times the patients would have been perfectly well if they had survived.

ROBERT R. LINTON, M.D.

Assistant Clinical Professor of Surgery, Harvard University Medical School; Senior Visiting Surgeon, Massachusetts General Hospital; Chief of the Peripheral Vascular Clinic, Massachusetts General Hospital.

TERMINOLOGY

There is a great deal in the medical literature about the terminology in regard to this disease. Ochsner [11] has popularized the term "phlebothrombosis" to designate the type of venous thrombosis which is more apt to result in pulmonary embolism, because the clot for the most part is unattached to the vein wall. (Fig. 1) Homans [9] has called this type "bland" venous thrombosis, whereas I prefer to call it "silent" venous thrombosis, because there is so little objective or subjective evidence that it exists until pulmonary embolism, either minor or fatal, occurs. The other type is called thrombophlebitis, because of the associated pain and tenderness over the course of the involved vein, the result of a sterile inflammatory process secondary to the thrombosis. The clinical picture is that of a large swollen extremity, the typical so-called phlegmasia alba dolens. The thrombus for the most part is adherent to the vein wall. (Fig. 1) It is my opinion that these two types of venous thrombosis are the same disease but represent different stages of it. It is true that the silent type is more apt to result in fatal pulmonary embolism, because the thrombus for the most part is unattached to the vein wall. Fortunately for many patients, however, this type of thrombosis may result in a typical phlegmasia alba dolens or thrombophlebitis without producing massive pulmonary embolism, resulting in the typically swollen leg of thrombophlebitis. (Fig. 1) That this may occur is borne out by the fact that not infrequently the patient, who has had no symptoms in the lower extremity until he gets out of bed, suddenly while walking experiences severe pain in one of his thighs and within a few hours the entire leg becomes discolored and swollen to the groin. Immediate femoral vein exploration with thrombectomy in such a case adds credence to this theory, since if the operation is performed within twenty-four or forty-eight hours after the leg becomes swollen and tender it will be found that the thrombus will be unattached and can readily be removed, whereas if the operation is postponed four to five days thrombectomy will be almost impossible because of the adherence of the clot. Although pulmonary embolism is less common in this stage of thrombophlebitis, it should not be forgotten that even fatal embolism may occur because of dislodgement of a propagated unattached thrombus in the iliac veins. For this reason, if for no other, femoral vein interruption with thrombectomy is the method of choice if the case is seen within forty-eight hours of the time the leg becomes swollen.

INCIDENCE

Thrombophlebitis, phlebothrombosis or venous thrombosis, whichever term is preferred, is usually considered to be a disease which affects primarily the surgical patient. This may be because surgeons have written so much about it in recent years, but this is not true apparently, since in our hospital a ten-year analysis of 45,000 patients admitted to the medical service revealed an incidence of thromboembolic disease of 0.6%, whereas in 98,000 admitted to the surgical service, the incidence was 0.24%, according to Carlotti et al [5]. These figures demonstrate that medical patients are more prone to develop the disease than the surgical patients.

We have been criticised in our hospital because we have reported so many cases of thromboembolic disease. There are a number of reasons I believe for this, and one is the increasing age of the patients admitted to the surgical service. Their mean age has been found to have increased from 36 to 40 years from 1930 to 1945, and furthermore more patients are seen now in the fifth, sixth and seventh decades of life, the ages when thrombosis and embolism are most common. Another reason for this high incidence in our hospital is that it is primarily a consulting hospital. We serve the local community to a certain extent, but most of the patients come from a considerable distance, referred because they need major surgical procedures which cannot be performed in the smaller community hospitals. Many of them are for extensive malignant disease and require operative procedures which were almost unheard of fifteen years

This paper was presented before the International Post-Graduate Medical Assembly, San Antonio, Texas, January, 1949.

ago. Both of these factors, it is believed, predispose to thromboembolism.

PROPHYLAXIS

Any discussion of thromboembolic disease is not complete without speaking of the prophylaxis. In order to understand this phase of the subject, one should fully realize which patients are most apt to develop it. An analysis of 367 patients with thromboembolic disease on the surgical services at the Massachusetts General Hospital revealed that 82 per cent were forty years of age or older. The same was found true on the medical service, as in a series of 273 medical patients with thromboembolic disease 87 per cent of them also were forty years of age or older.

(1) Anticoagulants

The use of the anticoagulant, dicumarol, deserves consideration in the prophylaxis of thromboembolism in surgical patients. It was used in 223 patients between forty and sixty years of age undergoing major surgical procedures at the Massachusetts General Hospital and omitted in a comparable control series. In this group nine patients developed evidence of deep venous thrombosis or pulmonary embolism, an incidence of four per cent. The control series of patients in the same age group undergoing similar operative procedures were not treated with it. In this group 45 instances of thromboembolism occurred, an incidence of approximately 20 per cent. These statistics indicate the value of the drug in reducing postoperative thromboembolic disease. The dosage of dicumarol used in these patients was relatively small, since the initial dose was 200 mg. given on the first postoperative day and if no elevation in the prothrombin time occurred in 48 hours, another 100 mg. was administered. Despite this small amount of the drug given prophylactically to 799 surgical patients, postoperative bleeding occurred in 22, or 2.7 per cent of the cases. (Table I). In 17 the bleeding was minor and in three it was major in amount, necessitating blood transfusions to control it, and in two it contributed to the patients' deaths. These statistics indicate that the drug is not without its dangers and furthermore it should not be administered unless there are adequate laboratory facilities for accurate prothrombin time determinations. Thromboembolism developed in 30 patients, or 4 per cent of this series of 799 treated with dicumarol, 16 had venous thrombosis and 14 nonfatal pulmonary embolisms. Bilateral femoral vein interruptions were performed in these 30 cases. It is of extreme significance that no deaths from massive embolism occurred in the entire group utilizing the combined prophylactic measures of dicumarol and femoral vein interruption in those cases that developed signs of venous thrombosis or minor pulmonary embolism.

(2) Prophylactic Superficial Femoral Vein Interruptions

Another method of prophylaxis that has been used in our hospital has been bilateral superficial femoral vein interruption before signs of thromboembolic disease have developed. The procedure was performed immediately before or after the major operation and in some cases at the same time. The majority of these patients were 65 years of age or over and in whom it was considered dicumarol was contraindicated. The procedure was performed in 871 patients. Venous thrombosis developed in 45, or 4 per cent of them. There were four deaths from massive pulmonary embolism, an incidence of approximately 0.5 per cent. In a comparable series of 871 patients who did not receive any specific prophy-

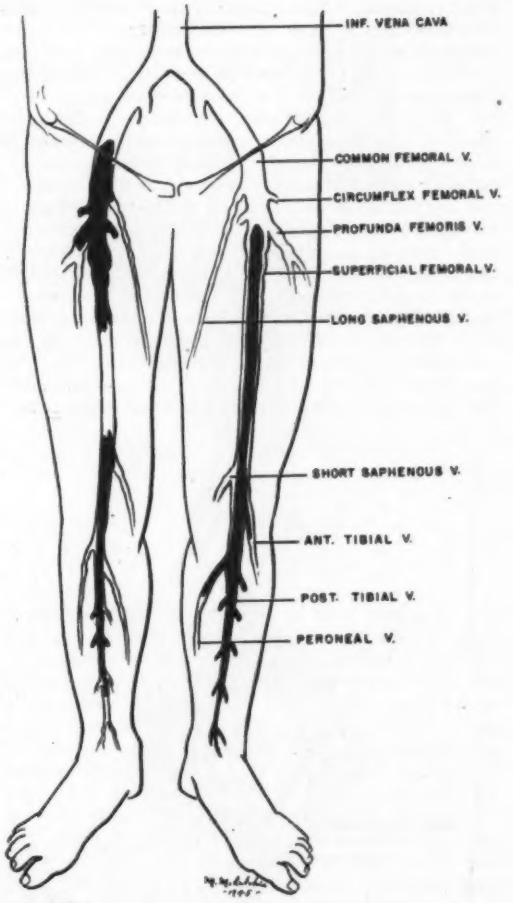

FIGURE 1. An artist's drawing of the deep veins of the lower extremities demonstrating phlebothrombosis and femoro-iliac thrombophlebitis. In the left leg is shown a long nonadherent thrombus in the femoral vein which has propagated from an area of thrombophlebitis in the veins of the calf... This is the so-called "silent" venous thrombosis, with few signs. The clot of this type may break off to produce fatal pulmonary embolism or as is shown in the right leg, the detached portion of the thrombus may lodge in the common femoral vein, occluding the collateral venous channels in this region to produce the classical picture of thrombophlebitis or phlegmasia alba dolens... Thrombectomy and common femoral vein interruption may be readily accomplished if carried out within 48 hours of the occurrence of this occluding thrombus.

(Courtesy Mason, Robert L., and Zintel, H. A.: Preoperative and Postoperative Treatment. By permission of W. B. Saunders Company, publishers, Philadelphia.)

lactic treatment, 102, or 12 per cent, developed venous thrombosis and 37, or 4 per cent, succumbed to massive embolism. It is obvious that the protection from this procedure is not one hundred per cent, nevertheless, these statistics indicate the value of prophylactic bilateral superficial femoral vein interruption in this older age group in whom postoperative thromboembolism is so frequently encountered. Because it did not prevent embolism in all the cases, however, it is planned to extend the use of dicumarol as a prophylactic measure in the older group of patients. Sufficient time to obtain a large series of patients so treated will be necessary to determine whether or not the hemorrhagic complications of the drug in this age group will outweigh its advantages. The fatalities from embolism following prophylactic femoral vein interruption have occurred for the most part in patients who have been bed ridden for long periods of time after the procedure was performed. For this reason if long continued bed rest becomes necessary because of unforeseen complications, it is advisable to administer dicumarol for its additional protection. If a patient can be made ambulatory within a short time after interrupting the femoral veins, this precaution is probably unnecessary.

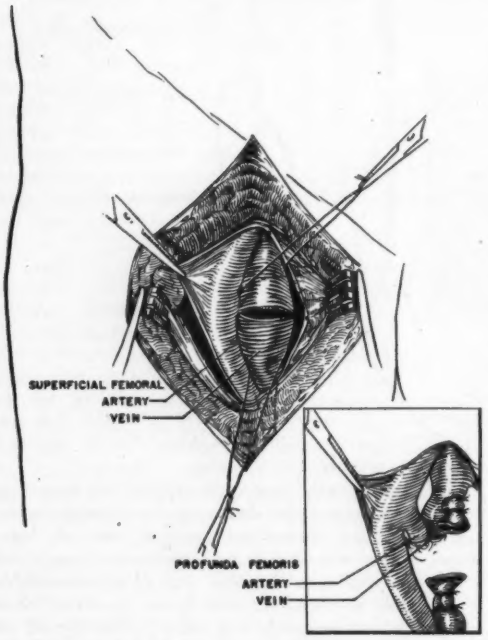

FIGURE II. Interruption of the superficial femoral vein. An artist's drawing to show the exposure of the right superficial femoral vein, using a vertical incision, the upper end commencing at the groin crease. The dilatation of the vein localizes the junction of the superficial and deep femoral veins. The femoral artery is retracted lateralward. The incision in the vein is indicated, and should always be transverse. The inset shows the divided superficial femoral vein with both ends doubly ligated. The ligatures on the proximal end should be placed as close to the deep femoral vein as possible, so that a blind segment of vein is not formed in which a secondary thrombus may develop and from which a pulmonary embolus might occur.

(Courtesy Mason, Robert L., and Zintel, H. A.: Preoperative and Postoperative Treatment. By permission of W. B. Saunders Company, publishers, Philadelphia.)

(3) Early Ambulation

Early ambulation is one of the most important prophylactic measures, especially for patients who can get out of bed within 24 to 48 hours after an operation. If this method is used it is essential that when the patient is up he must be walking and not sitting in a chair, because the latter tends to favor venous thrombosis. Failure to follow this rule may, in part at least, explain the increased incidence of thromboembolic disease reported by Blodgett et al [4] in patients in whom early ambulation was practiced. My own rule is that early ambulation means that the patient either lies down or walks for the first five or six postoperative days. An additional advantage of this routine is that muscles do not weaken from disuse so that patients may be discharged earlier from the hospital. It should be pointed out, however, that this method will not prevent venous thrombosis in all cases, so that frequent examinations of the lower extremities should not be neglected.

THERAPEUSIS

(1) Anticoagulants

Heparin was the first effective anticoagulant recommended for the treatment of thromboembolic disease either before or after pulmonary embolism had occurred. Its chief disadvantages are the difficulty of administration and the expense of the drug. The chief advantages are that a prolongation in the coagulation of the blood can be obtained almost immediately after administration and likewise the effect of it, if it must be discontinued, disappears in a few hours. If a more rapid neutralization is demanded, protamine may be given, since this almost immediately counteracts the drug. If heparin is administered, the blood coagulation time, utilizing the multiple tube method, should be determined and the clotting time maintained somewhere between 20 and 30 minutes. The drug is not without its dangers in the surgical patient following operation even when the blood coagulation time is kept within this time. I have had one death from postoperative hemorrhage following a lumbar sympathectomy. **Dicumarol** is the anticoagulant which is in vogue at the present time. The chief advantages of it are the ease of administration, unless the patient cannot be fed by mouth, and its cheapness. The disadvantages are the delay in action, as it requires 48 hours as a rule to take effect; second, the difficulty of counteracting it in case of overdosage, and third, the difficulty in the smaller hospitals especially of maintaining satisfactory laboratory facilities to determine accurately the prothrombin time.

Numerous statistics have been published indicating the value of these drugs in many cases. From each clinic (Table II), however, a varying number of fatal pulmonary emboli are reported so that this method in itself does not afford protection in all cases. The failure of heparin to protect all patients with recognizable deep venous thrombosis from fatal pulmonary embolism was demonstrated to me in 1940 by the following case: A man, aged 41 years, developed typical postoperative femoro-iliac venous thrombosis following a spinal fu-

sion. Adequate anticoagulant therapy was administered by a continuous intravenous drip of heparin solution for a period of 15 days. Massive pulmonary embolism with sudden death occurred on the 16th day, just 24 hours after the drug had been discontinued. Postmortem examination in this patient revealed that the fatal embolism was a portion of the thrombus from the iliac vein on the same side that the thrombophlebitis was recognized. One might be criticized for discontinuing the anticoagulant before this patient was ambulatory and that the fatal embolus was a clot which had formed following the cessation of heparin administration. The postmortem examination revealed, however, that the fatal embolus was an old and partially organized thrombus which antedated the discontinuance of the anticoagulant by many days. It is believed that if bilateral femoral vein interruption with thrombectomy had been performed instead of relying on the anticoagulant heparin, this patient would still be alive. Based on this case and similar ones subsequently observed, it is believed that once the diagnosis of venous thrombosis with or without a warning minor pulmonary embolus has been established bilateral femoral vein interruption is recommended as the best method of treatment. If desired the anticoagulant dicumarol may be given for additional protection.

(2) **Sympathetic Nerve Block**

The paravertebral injection of the lumbar sympathetic nerves with procaine solution, as advocated by Ochsner [12], is of chief value in patients with the obstructing type of iliofemoral thrombosis to relieve pain and edema. The chief drawback to this method of therapy is that it does not protect the patients from pulmonary embolism, either minor or fatal.

(3) **Venous Interruption**

Homans [10] in 1934 first reported the procedure of femoral vein interruption for the treatment of deep venous thrombosis of the lower extremity with pulmonary embolism. Since then it has been advocated in many clinics, but the largest series of patients subjected to this method of therapy has been reported by Allen et al [1] from the Massachusetts General Hospital. The first patient so treated in this clinic was in 1937. During the 12 year period from 1937 to 1948 inclusive, 1450 patients have had one or both femoral veins interrupted for the therapeusis of thromboembolic disease and 1,041 for prophylaxis, a total of 2,491 patients. These figures indicate the tremendous effort expended in an attempt to reduce the morbidity and mortality rate of this disease. In the beginning if signs of venous thrombosis were present only in one extremity, the venous interruption was performed only in it. However, with further experience in this and other clinics, it became apparent that bilateral interruption should be done even though the diagnosis of thrombosis could only be made in one extremity. This is chiefly because the disease is so treacherous that fatal emboli have occurred from the supposedly normal, unaffected leg, so that during the past five years bilateral interruptions have been performed almost routinely at the same operative procedure.

The indications for this method of therapy are threefold. The first and perhaps the most important is that it should be performed on any patient who has had a minor or nonlethal pulmonary embolus. The development of sudden chest pain followed later by the characteristic findings of pleural friction rub with pain on breathing are classical signs of this condition. The occurrence of hemoptysis in addition is practically pathognomic of pulmonary infarction. The diagnosis may be further substantiated by anteroposterior and lateral roentgenograms of the chest. Since the majority of pulmonary emboli, as high as 95 per cent, according to some authorities [8], arise from the deep veins of the leg, it is our opinion that if the diagnosis of a minor pulmonary embolism or infarction is made, bilateral femoral vein interruption should be performed even **if no signs of venous thrombosis in the extremities are detectable.** In support of this opinion Welch and Faxon [14] reported a mortality rate from massive pulmonary embolism of approximately 25 per cent in the group of patients who had had previous small or warning pulmonary emboli. The second indication for femoral vein interruption is the development of signs of venous thrombosis in the deep veins of the lower extremities. The morbidity of thromboembolic disease can be greatly reduced

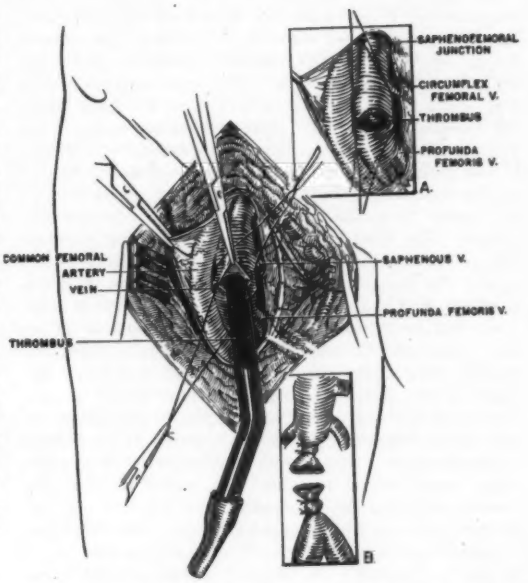

FIGURE III. Interruption of the common femoral vein with thrombectomy. An artist's drawing to show the exposure of the right common femoral vein. The upper end of the incision should be 2 cm. above the groin crease. The femoral artery is retracted lateralward. Two untied ligatures have been placed around the vein to control the bleeding after thrombectomy. The thrombus is removed by aspiration through a glass cannula. The proximal segment is always aspirated first. Inset A, shows the thrombus protruding through the transverse incision in the vein. Inset B, shows the completely divided vein with both doubly ligated with nonabsorbable ligatures. The division is above the junction of the superficial and femoral veins.

(Courtesy Mason, Robert L., and Zintel, H. A.: Preoperative and Postoperative Treatment. By permission of W. B. Saunders Company, publishers, Philadelphia.)

if the diagnosis can be made early and the femoral veins interrupted. If the thrombus has extended to involve the femoro-iliac veins, resulting in edema of the extremity up to the groin, the procedure should be performed with thrombectomy providing the patient is seen within forty-eight hours of the development of the thigh swelling. Operation after the elapse of a longer period, three days or more, is very unsatisfactory because the thrombus becomes so adherent to the vein wall that it cannot all be removed, especially the proximal portion which will result in pulmonary embolism if it becomes dislodged. The third indication for femoral vein interruption is believed to be the development of a concomitant rise in the temperature, pulse and respiration in a patient who has had a normal chart and in whom no other cause can be found to explain these findings. It is believed that the elevation in these three vital signs frequently indicate the lodgment of a small pulmonary embolus so that bilateral femoral vein interruption is justifiable, irrespective of what the extremities show on physical examination. When it is necessary to perform a thrombectomy, supplementary treatment with dicumarol is recommended to reduce the formation of a secondary thrombus both proximal and distal to the site of interruption. This seems to be a worth while precautionary measure, as femoral vein interruption is not a perfect operation to prevent pulmonary embolism, since a secondary thrombus may form in the proximal end of this vessel which may be large enough, if it becomes dislodged, to produce sudden death from massive embolism. This is especially true when a thrombus has been removed, since another may readily form because of the intimal damage secondary to the initial thrombosis and also the mechanical procedure of removing it.

(4) Technic of Femoral Vein Interruption

The operation of femoral vein interruption is regarded by many as a simple surgical procedure. This is perhaps due to the fact that it is performed frequently under local procaine infiltration anesthesia. It should be stressed, however, that **the operation should be performed only by a surgeon experienced in the surgery of major blood vessels.** The average surgeon, before attempting the procedure, should make a special study of the anatomy of the femoral artery and vein with their tributaries by careful dissections of the femoral triangle, preferably in the postmortem room. The fundamental vascular surgical principle that an incision to expose a major blood vessel lie directly over and parallel to it, must be rigidly followed, since it gives the most adequate exposure—something that is extremely necessary if the femoral vein is accidentally wounded. An oblique incision with its limited exposure of the femoral blood vessels was used in three patients who have been seen that lost extremities due to inadvertent injury to the femoral artery. These were performed by surgeons outside our hospital. Contrasted to these calamities, we have performed femoral vein interruptions on 2,491 patients up to January 1, 1949, and in the majority the procedure has been done in both extremities, making a total of approximately 4,000 interruptions of a femoral vein without injury to the arterial blood supply of the limb. The vertical type of incision parallel and directly over the femoral vessels has been utilized in all cases. The poorer cosmetic appearance of the scar, as compared to the oblique incision which parallels the cleavage planes of the skin, is far outweighed by the more adequate exposure, so that if hemorrhage is encountered from inadvertent wounding of the femoral vein, additional exposure to control it may readily be obtained both proximal and distal to the injury. Due to the fragile nature of major arteries, especially in individuals beyond middle life, the femoral artery should not be isolated and retracted with rubber tubing, tape or retractors. Gangrene necessitating amputation of the leg has been observed in one patient secondary to arterial thrombosis due to fracture of the arterial wall from retraction of the vessel with a rubber catheter.

The incision should extend from the crease in the groin distalward about 8 to 10 cm., the length depending a little on the degree of obesity of the patient. The inguinal lymph nodes are usually encountered and may be retracted medialward or lateralward. The fascia of Scarpa's triangle is then recognized. It is incised to expose the femoral blood vessels which are encased in a vascular sheath. The femoral vein lies medialward and somewhat posterior to the artery. Retraction of the artery is obtained by placing the end of the retractor in close proximity to it but not on it, and thus the artery is usually drawn lateralward to expose the femoral vein. (Fig. 2) If a thrombus is found within the femoral vein, the interruption of this blood vessel should be proximal to the profunda femoris branch and distal to the saphenofemoral junction. (Fig. 3) An incision is made transversely in the vein wall and the proximal end of the vein aspirated utilizing a glass tube until free bleeding is obtained. The distal end is also aspirated, although this is not so imperative. The advantage of the latter step is that collateral venous channels may be unplugged by removing the thrombus, and thus the post-thrombotic edema may be greatly reduced. As a rule, if the common femoral vein is interrupted, it is necessary

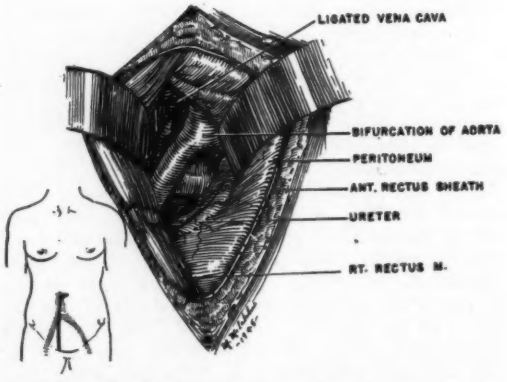

FIGURE IV. Interruption of the inferior vena cava. An artist's drawing to show the extraperitoneal exposure and ligation in continuity of the inferior vena cava, using a right paramedian incision. The rectus muscle is retracted lateralward and the ureter, peritoneum and its contents medialward. The incision extends from the pubis to about 5 centimeters above the umbilicus. For ligation, we use two nonabsorbable ligatures of silk or cotton.

(Courtesy Mason, Robert L., and Zintel, H. A.: Preoperative and Postoperative Treatment. By permission of W. B. Saunders Company, publishers, Philadelphia.)

to separately ligate and divide a tributary of the common femoral vein, usually the lateral femoral circumflex vein. (Fig. 3) This is necessary in order to get sufficient length of vein to safely ligate and divide the common femoral vein. Some surgeons prefer to ligate it in continuity, but it is believed that the procedure of choice is a ligation and division. Both ends of the common femoral vein should be doubly ligated, first with a heavy silk or cotton ligature and distal to it in each end of the vein, a transfixion suture of the same material.

The common femoral vein should never under any circumstances be interrupted proximal to the saphenofemoral junction. This is especially true in elderly people who have poor arterial circulation. One patient has been observed who lost his leg following interruption at this level because there was insufficient venous collateral to permit blood to return from the leg to the trunk. In our clinic the majority of interruptions have been of the superficial vein just distal to the profunda femoris. Due to the fact that we have had a certain number of fatal embolisms arising from thrombi originating in the profunda femoris branch, it is my rule at the present time to interrupt the common femoral veins (1) in those patients in whom thrombi are found in the femoral vein, (2) in cardiac patients and others who must stay in bed for long periods of time even though no thrombi are found. The superficial femoral vein, on the other hand, is interrupted in young people in whom signs of venous thrombosis are limited to the lower leg and in most instances of prophylactic femoral vein interruption where the patient does not have a long period of bed rest following the operative procedure.

(5) Inferior Vena Cava Interruption

Venous interruption at a higher level is necessary in some patients. The most effective level to perform this is of the inferior vena cava distal to the renal veins and just proximal to the junction of the common iliac veins. It should not be performed in preference to femoral vein interruption, since it carries a much higher mortality rate, as shown by the statistics of Thebaut and Ward [13]. It is a major operative procedure requiring general anesthesia in contradistinction to femoral vein interruptions which may be done under local procaine anesthesia. The chief indications for interrupting the inferior vena cava are (1) septic pulmonary emboli arising from a septic thrombophlebitic process in the pelvis, (2) in patients who, following interruption of the femoral veins and additional dicumarol therapy, still have repeated pulmonary embolic episodes. In our clinic this procedure has been done only in a few patients. Compared to approximately 2,500 patients who have had femoral vein interruptions, we have only interrupted the inferior vena cava in approximately 20 patients. It is a life saving procedure, however, and certainly should be utilized in the rare case where femoral vein interruption and the anticoagulant therapy are not sufficient.

The most satisfactory method to expose the inferior vena cava is obtained by utilizing a right paramedian abdominal incision, extending from the pubis to about two inches above the umbilicus. (Fig. 4) The rectus muscle is retracted lateralward and the peritoneum and its contents are rolled up out of the iliac fossa. The bifurcation of the inferior vena cava is almost at the level of the umbilicus, so adequate exposure is essential in the cephalad direction. Since the inferior vena cava is

TABLE I.
COMPLICATIONS OF PROPHYLACTIC DICUMAROL IN 799 PATIENTS
Massachusetts General Hospital
1945-1948

	With Response	Without Response	? Response	Total
*Minor Bleeding	17	0	0	17
*Major Bleeding	3	0	0	3
**Phlebitis	6	6	4	16
**Infarct	9	0	5	14
Fatal Pulmonary Embolus	0	0	0	0
Deaths from Delayed Hem'rrh'ge	1	1	0	2

*—Requiring Vitamin K and Transfusions
**—Requiring Femoral Vein Interruption.

TABLE II.
MORTALITY FOLLOWING THERAPEUTIC MEASURES IN THROMBIC-EMBOLIC DISEASE

		Measures	No. of Cases	Deaths from Emb.	Mortality Rate
Zilliacus [15]	(1946)	Anticoagulants	576	3	0.52%
Bauer [3]	(1946)	"	209	3	1.4
Evans [7]	(1948)	"	127	3	2.4
E. V. Allen [2]	(1947)	"	572	1	0.17
Cumine [6]	(1948)	"	89	2	2.2
M. G. H.	(1949)	Fem. Vein Int.	1450	7	0.48

such a large blood vessel and it would necessitate isolating a considerable length of it to safely ligate and divide it, ligation in continuity has been resorted to in the cases done in our clinic. The interruption has usually been with No. 0 braided silk, using two ligatures about one centimeter apart. In patients with septic lower abdominal incisions from previous surgery, the vena cava may also be approached through the flank, using a kidney type of incision. This exposure is not quite as satisfactory as the anterior one, but in some cases must be used of necessity. No serious sequelae have been observed immediately following interruption of the inferior vena cava to the extremities. What the long term result will be, it is difficult to state. In two patients that I have operated on I have interrupted the femoral veins as well as the inferior vena cava without serious sequelae over periods of three and five years in these patients. Further time, however, is necessary in order to determine if chronic ulcerations and dermatitis are more apt to develop than after femoral vein interruption.

SUMMARY

An analysis of thromboembolic disease at the Massachusetts General Hospital treated by various means from 1937 to 1948 reveals that prophylactic dicumarol has been used in 799 patients with two deaths from hemorrhage related in part at least to the drug, a mortality rate of 0.25 per cent. Prophylactic superficial femoral vein interruption was utilized in 1,041 with five deaths, a mortality of 0.5 per cent. Therapeutic femoral vein interruption with thrombectomy where indicated was performed in 1,450 patients with seven deaths, a mortality rate of 0.8 per cent. From these statistics it will be seen that we do not have a method of preventing deaths in all patients, either by the present prophylactic

or therapeutic measures. The results in our clinic by femoral vein interruption correspond very favorably and possibly show some improvement over those clinics where the anticoagulants have been used exclusively. (Table II) It is obvious that further study and research are necessary. The ideal anticoagulant as yet has not been discovered and the answer may not lie entirely in this direction, since it seems possible that the degeneration of the venous wall and the intima, similar to that seen in arterial thrombosis, may be the chief etiological factor in many cases of venous thrombosis, especially in the aged. It is because of this fact, namely, that phlebosclerosis is almost as common as arteriosclerosis in the aged, that I feel femoral vein interruption, if properly performed, carries a lasting benefit that is not obtained from the use of the anticoagulants, which of necessity must give only temporary benefit while the drug is being administered. It is our opinion at the present time, however, that a combination of femoral vein interruption and the use of the anticoagulants will give the best results in many cases, and in some interruption of the inferior vena cava may be necessary in addition to protect the patient from massive pulmonary embolism. The anticoagulants in our opinion should be used primarily as a prophylactic procedure rather than as a therapeutic one.

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Albuquerque Medical News

On June 17 there was a meeting of representatives from the various hospitals, civic and county groups, and the New Mexico Department of Public Welfare to consider the critical hospital deficits which have been accruing in the Albuquerque area.

It appears that financial difficulties have been created largely by the loss sustained through caring for welfare cases for fees granted by government agencies, considerably below actual cost to the hospitals. Additional attrition results from caring for many accident cases for which payment is never made.

A committee was appointed further to study the situation which is particularly ominous for several reasons. Albuquerque, during the past few years, has been in a favored position financially because of the high rate of employment resultant from its government projects. Despite this, the hospitals have been operating with increasing deficits.

Since philanthropy can no longer be counted on to make up these losses because of increased taxation, and in the face of receding business activity at present, it appears that the governmental agencies which have asserted and even insisted on their responsibilities in these matters for purposes of taxation, should accept their responsibilities for purposes of service.

Meanwhile, it should give pause for thought to those proponents of the welfare state as to whether failure on the small scale of adequately caring for the indigent is a likely portent of success on the large scale of taking care of all of us.

Dr. R. W. Mendelson of Albuquerque, long regarded as one of the foremost internists in this area, and formerly vice-president of the Southwestern Medical Association, has retired from private practice to return to active service with the Army Air Force. He has just been assigned as surgeon to the 81st Fighter Wing at their new base at Kirtland Field in Albuquerque.

The U. S. Veterans Hospital in Albuquerque has had its resident staff replenished as part of training program under the jurisdiction of the University of Colorado Medical School. Plans for training physicians in the medical specialties utilize not only an excellently qualified full time staff, but also local private practitioners.

Not only members of the Veterans Hospital staff, but the medical profession in the area at large have benefited by the lecture program which has been formulated and integrated in part with the efforts of the New Mexico Clinical Society. Through the good offices of both these organizations, Albuquerque has been favored with such eminent lecturers as Dr. Isaac Starr, Dr. William Dock, Dr. Hans Selye, and others.

A chapter of the American Heart Association is in the process of being formed in New Mexico. Some units of this chapter are already functioning. An organizational meeting is being planned for September 8, in Albuquerque, at which time several directors from the central organization will meet with members in this area. All physicians interested in participating in the activities of this group are invited to direct their inquiries to this correspondent or Dr. H. L. January of Albuquerque.
—ROBERT FRIEDENBERG, M.D., Albuquerque, N. M.

PROTHROMBIN AND DICUMAROL

By RITA L. DON, B.A., M.T. (ASCP)

It cannot be too strongly emphasized that the administration of Dicumarol must be based on the value for prothrombin in the blood. Any other program may lead to serious hemorrhage or to inadequate control of coagulation. Identical amounts may produce widely dissimilar effects on prothrombin when administered to different persons. Indeed, the prothrombin of the blood of the same person may be affected dissimilarly by the same amounts of Dicumarol given on one or more than one occasion. The drug requires daily determination of prothrombin levels, and accurate and consistent results are imperative if the patient is to be adequately treated.

I make a plea for the discontinuation of reporting prothrombin time. Since thromboplastins vary in potency, to bring about uniformity, every laboratory should report the prothrombin not in seconds but in percentage of normal. At the very least, reports should contain the prothrombin time for three critical values of prothrombin, 30 per cent, 20 per cent, and 10 per cent.

One may administer the drug adequately knowing only these figures; for clinical experience has indicated that intravascular thrombosis rarely occurs when the percentage prothrombin in the blood is less than 30, and bleeding rarely occurs when the percentage is 10 or more.

THE PROTHROMBIN TEST

One will find numerous methods for the determination of prothrombin, reviewed in the literature, all of which have many advantages. In our laboratory we have found that the one-stage methods are practical, consistent, and reliable, if the utmost care is taken in technique. This is one laboratory procedure where there is absolutely no room for error. All one-stage prothrombin tests today are based on the original method of Quick.

Regardless of the method used, each laboratory should determine its own dilution curve in order to report accurately in per cent of prothrombin. Variations in the strengths of the thromboplastin and other factors will make it impossible to read results from dilution curves that have been made in other laboratories. In the following outline of the method we followed closely the Link and Shapiro modification.

Reagents:

1.) M/10 Sodium Oxalate.

Dissolve 1.34 gm. of sodium oxalate in enough distilled water to make a total of 100 c.c.

2.) M/40 Calcium Chloride.

Dissolve 0.28 gm. of anhydrous calcium chloride in enough distilled water to make a total of 100 c.c.

3.) Thromboplastin Solution.

Difco Laboratories Inc. Bacto-thromboplastin is used in our laboratory. Thromboplastin of the same lot number possess similar activity. It is stored in a refrigerator at 4° C. When ready for use 0.15 gm. of thromboplastin is placed in a test tube containing 0.05 c.c. of M/10 sodium oxalate to which is added 2.5 c.c. of normal saline. After the test tube is thoroughly shaken to insure uniform distribution of particles, it is placed in a water bath maintained at 45° C. for exactly ten minutes. While in the water bath, the test tube is vigorously shaken for ten seconds every two minutes. It is important that the material be shaken regularly and consistently at the two-minute period, as the amount of agitation will change the prothrombin obtained.

At the end of the incubation period the thromboplastin extract is drawn through a cotton plug at the end of a pipette and used for testing. If the thromboplastin solution is not to be used immediately it should be kept in the refrigerator (4° C.) until the test is to be run. The thromboplastin solution should be prepared fresh each day.

Technique:

1.) Preparation of Blood Specimens.

Plasma for prothrombin determinations is obtained by mixing 4.5 c.c. of venous blood, taken with a dry syringe, with 0.5 c.c. of M/10 sodium oxalate. This is centrifuged at 1,500 r.p.m. for ten minutes. All determinations should be completed within an hour after the blood is drawn.

2.) Determination of Prothrombin Time.

All materials and solutions to be used in the performance of the test are placed in a water bath in a hot air oven at 37° C. for ten minutes. With the right hand place 0.1 c.c. of M/40 calcium chloride into a test tube in the rack in the water bath, add 0.1 c.c. of thromboplastin solution and mix, finally add 0.1 c.c. of plasma and at the same instant the stopwatch is started with the left hand. The prothrombin testing tube is picked up with the right hand and tilted continuously while being held with its contents clearly visible yet barely submerged in the water bath. The instant the first strands of fribrin appear, the watch is stopped, and the prothrombin time recorded to the nearest tenth of a second. Determinations are made in duplicate and averaged.

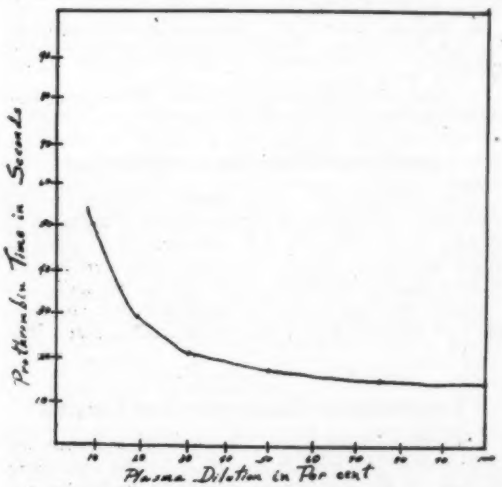

Fig. I. Normal Plasma Prothrombin Dilution Curve.

3.) Preparation of Prothrombin Dilution Curve.

The plasma from five normal individuals is pooled.

Then the prothrombin time is determined on this pooled serum in the dilutions 100 per cent, 75 per cent, 50 per cent, 30 per cent, 20 per cent, and 10 per cent. The dilutions are made with normal saline. From these results a curve is plotted on graph paper as show in Fig. I. The prothrombin time of unknown plasma may now be interpreted in per cent of normal from this curve. For each new lot of thromboplastin a new curve must be made because of the variance in potency.

SUMMARY

1. The importance of determining prothrombin levels when Dicumarol is administered to a patient is stressed.

2. The prothrombin test as devised by Quick and modified by Link and Shapiro is reviewed in detail with certain precautions emphasized:

a.) The test should be performed with the utmost of accuracy.

b.) The blood should be drawn with a dry syringe. Hemolysis shortens the prothrombin time.

c.) The test should be run within an hour after the blood is withdrawn. The prothrombin activity deteriorates the longer the blood stands.

d.) The thromboplastin solution should be prepared fresh each day. If the solution is not to be used immediately it should be kept in the refrigerator (4° C.).

e.) The dried thromboplastin should be stored at 4° C.

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2. Martin, John W.; Curfman, George H.; Cavano, Frank L.;—The Prothrombin Time and Variables in the Method; J. Lab & Clin. Med. 32: 554-565 May '47.

3. Barker, Nelson W.; Hurn, Margaret; Magarth, Thomas B.;—The Determination of Prothrombin following administration of Dicumarol; J. Lab & Clin. Med. 30: 432-447 May '45.

4. Aggler, Paul M.; Standardization of the Quick Prothrombin Time; Blood 1: 220-233 May '46.

Southwest New Mexico Meeting

The Southwestern New Mexico Clinical Society meeting at the Veterans Administration Hospital, Fort Bayard, N. M., July 22, was addressed by Dr. John B. Grow, of Denver, Colo., on certain aspects of thoracic surgery, and by Dr. Rosenblatt of the hospital staff, who discussed the current status of streptomycin in the treatment of tuberculosis.—E. A. RYGH, M.D., Santa Rita, N. M.

Treatment of Tendinitis And Bursitis

"Roentgen therapy was the most favored conservative measure and was considered . . . to be satisfactory in cases of acute or chronic calcific or noncalcific tendinitis or bursitis. Sometimes symptoms rapidly subsided and calcium deposits disappeared. Results were best in acute cases or in chronic cases in which the deposits were soft, fuzzy and small, less notable in chronic cases or in acute cases with large, dense, discrete deposits. Roentgen therapy dilates capillaries, increases their permeability, leads to phagocytosis of fibrin and necrotic tissue. The effect is not a direct one on the deposits."—Hench, P. S., **et al, Ann. Int. Med.** 28:309, 1948.

New York Tumor Specialist To Address El Paso Groups

Dr. Norman L. Higginbotham, assistant director of medical education and director of the Bone Tumor Clinic Memorial Hospital, New York, and instructor in surgery at Cornell University Medical School and New York University, will be the guest of the Tumor Clinic of El Paso County Medical Society, Sept. 13.

Doctor Higginbotham will attend the meeting of the Tumor Clinic, 408 East Overland Street, El Paso, at 1 p. m. Sept. 13, for case presentation or bone tumors. That night at 8 o'clock, he will present a paper on "Malignant Bone Tumors—Some Practical Considerations", before a meeting of El Paso County Medical Society at 1301 Montana Street. All physicians are invited to attend both sessions.

Doctor Higginbotham is a diplomate of the American Board of Surgery and a member of numerous national and international medical societies. His works have been widely published in American medical literature.

Doctor Higginbotham is personally well known throughout the Southwest and Texas. As a colonel during World War II he was for four years chief of surgical service at Regional Hospital, Camp Swift, Texas; and he was commanding officer of the same hospital from Nov. 15, 1945, to Feb. 1, 1946.

There are numerous physicians in El Paso and the Southwest who served in Doctor Higginbotham's command and who will be present to greet and hear this distinguished physician Sept. 13 in El Paso.

Report Of The Committee For The Evaluation Of Anticoagulants In The Treatment Of Coronary Thrombosis With Myocardial Infarction

"On the basis of data compiled from 800 cases of coronary occlusion with myocardial infarction, it is concluded that:

"1. Patients treated with anticoagulant therapy in addition to the conventional forms of therapy experience a death rate and incidence of thromboembolic complications during the first six-week period following an attack which are markedly lower than those experienced by patients treated solely by conventional methods.

"2. Anticoagulant therapy should be used in all cases of coronary thrombosis with myocardial infarction unless a definite contraindication exists.

"3. In the absence of other hemorrhagic states, the hazards from hemorrhage due to anticoagulants are not sufficient to contraindicate their use in the treatment of coronary occlusion providing there are facilities for adequate laboratory and clinical control."—Wright, I. S., Marple, C. D., and Beck, D. F., **Am. Heart J.** 35:815, 1948.

Renal Infarction

"The most important single item in diagnosis of acute infarction of the kidney in complete, or almost complete, loss of function, almost irrespective of the degree of tissue involvement, in kidneys in which pyelography remains unchanged. Chronic infarction is recognizable in proportion to the caliceal atrophy which results from the infarct in its scar stage."—Regan, F. C., and Crabtree, E. G., **J. Urol.** 59:981, 1948.

SOME DIAGNOSTIC PROBLEMS OF CHRONIC PULMONARY DISEASES**

By H. Corwin Hinshaw, M.D., Rochester, Minn.

There has been an unprecedented upsurge of interest in the diagnosis and treatment of thoracic diseases during the past decade. This has been related to the solution of certain surgical problems which developed during the recent war and especially to the development of the antibiotics and to the perfection of photofluorographic methods of mass roentgenography.

Most physicians now in practice have witnessed the conquest of pneumococcal pneumonia and now see promise of an effective agent against some of the non-bacterial ("virus") pneumonias. Patients who would have died a physiologic (anoxic) death are now saved by efficient devices for administration of oxygen. Others who might have died as a result of the infection are saved by antibacterial and antiviral drugs.

The management of chronic infectious thoracic diseases such as pulmonary abscess, empyema, and bronchiectasis has changed utterly in recent years. Medical treatments now avert surgery more frequently, and when surgery is required, it is more safely and more effectively performed. Internists and surgeons have learned anew of their intimate interdependence upon each other and of their need for well-trained laboratorians and anesthetists.

INCREASE SEEN

Malignant pulmonary diseases, especially bronchiogenic carcinoma, are apparently increasing in incidence and in interest. It is now one of the most frequently encountered cancers in the male sex, and advances in surgical therapy offer a distinct ray of hope to the victim; a ray which may broaden to a beam within another decade or two.

Tuberculosis, that most significant of chronic infectious diseases of the human race, is confronted with new weapons of diagnostic and therapeutic power. Not only has the physician come into the possession of new methods of combatting tuberculosis, but he is ever becoming more adept in the use of older methods of diagnosis and treatment. Antibiotics effective against the tubercle bacillus combined with more discriminating use of collapse therapy and occasionally actual removal of diseased pulmonary tissue has regenerated a laggard field of medical endeavor.

The physician frequently is confronted with some evidence of thoracic disease and finds it difficult to determine what investigations are warranted. Therefore I have chosen to list some of the common situations which prompt the patient to seek medical advice because of suspected chronic pulmonary disease, and I shall make some suggestions as to those methods of study most likely to yield helpful information.

SHADOWS OBSERVED

Abnormal shadows are observed occasionally on chest roentgenograms of persons without thoracic complaints. This is more frequent in this day of mass x-ray surveys and routine x-ray examination of patients in hospitals and physicians offices. It has become well established that routine roentgenographic examination is a justifiable procedure even when symptoms of thoracic disease are lacking. This has become one of the most significant developments in the practice of preventive medicine, rivaling in importance the routine blood and urine tests so universally performed. It is difficult at times to persuade patients of the potential threat of undiagnosed asymptomatic pulmonary disease, and it is very frequently difficult or impossible to arrive at a satisfactory diagnosis without extensive and prolonged study.

The character and location of abnormalities observed on films of the chest may lead the experienced observer to suspect either tuberculosis, malignant tumor, acute pulmonary inflammation, or rarer miscellaneous conditions. The astute diagnostician will rarely attach an etiologic label to a lesion on the basis of roentgenographic evidence alone, but will demand more direct proof. When tuberculosis is suspected, tuberculin tests should be applied, and if results are negative, this disease is usually excluded from further serious consideration. Positive tuberculin tests are, of course, less significant under most circumstances. The diagnosis of active tuberculosis is rarely absolute without identification of the bacillus, and fortunately this can be accomplished much more frequently now than in former decades. Inactive, latent pulmonary tuberculosis may be a serious threat to the patient's future and frequently requires prolonged observation by serial roentgenograms for many years or even for the patient's lifetime. Changing lesions, whether improving or progressing, are more significant than lesions which remain stable over the years.

PROMPT INVESTIGATION

Shadows on roentgenograms of the chest which suggest malignant tumors demand prompt and thorough investigation. Bronchoscopic examination frequently is required and cytologic examination of secretions should be undertaken if such facilities are available. Diagnostic thoracotomy is more frequently resorted to in recent years and should be considered when the experienced diagnostician fears malignant disease but cannot prove it otherwise. He must weigh the risk of operation in comparison with the risk associated with delayed diagnosis. When classical x-ray signs of pulmonary malignancy appear, the disease has too frequently progressed beyond the stage of operability.

Symptoms and findings of pneumonia may be the result of an obstructing bronchiogenic carcinoma, and recurrent pneumonia in the same lobe or segment always arouses suspicion of bronchial obstruction. I believe that each patient with pneumonia should be observed by x-ray until the shadow disappears. This is especially true of males in the cancer age range. Bronchiogenic carcinoma is very much rarer in women and younger individuals, but occasionally an adenomatous tumor of a bronchus may produce obstructive pneumonia in such persons. Pulmonary abscess also frequently is caused by bronchiogenic carcinoma and must not be dismissed without complete examination to exclude this possibility. Obstructive pulmonary inflammation produced by car-

cinoma may respond temporarily to penicillin therapy as dramatically as does lobar pneumonia and mislead the clinician into serious delay.

COUGH AND EXPECTORATION

Cough and expectoration are utterly nonspecific symptoms but deserve serious consideration, especially if persistent and progressive. Often the history alone will strongly suggest bronchiectasis, asthmatic bronchitis, or the functional habit cough of the tense, nervously unstable individual. Bronchographic studies with iodized oil usually are required when the bronchiectasis is suspected, and methods of bronchography have greatly improved in recent years. Bronchographic visualization of each broncho-pulmonary segment is necessary before pulmonary resection for bronchiectasis is considered.

Hemoptysis is a justifiable cause for alarm by patient and doctor. Every reasonable effort should be made to explain the reason for hemoptysis and usually this can be accomplished successfully. Frequently it is necessary to resort to bronchoscopy and bronchography in addition to usual roentgenographic and bacteriologic investigations.

The symptoms of stridor and persistent hoarseness often require thorough examination of the lungs as well as of the larynx. Dyspnea is a symptom difficult to analyze but often a carefully detailed history and physical examination will reveal whether the basis is cardiac or pulmonary.

Pleural effusion always signifies serious disease and an exact etiologic diagnosis should be sought assidiously, and if not found, tuberculosis should be the working diagnosis. Tuberculous effusions may be associated with very abrupt symptoms, closely simulating those of an acute infection and leading to suspicion of pneumonia with pleurisy.

BAFFLING SYMPTOMS

Thoracic pain is often a baffling symptom arousing great apprehension, even when not due to serious disease. Vague, shifting, recurrent aching distress in the chest is a very common symptom in healthy individuals and may well belong to that troublesome assortment of "rheumatic" complaints. When thorough examination reveals no disease and confident reassurance is given by the physician, this symptom often nearly or quite disappears, lending confirmation to the belief that the psychosomatic factor is important. To call all vague thoracic pains "pleurisy" is a serious misnomer in my opinion. The symptoms of true pleuritis are not difficult to recognize and may signify such serious diseases as pulmonary embolism, pneumonia, tuberculosis, or malignant disease.

Most thoracic complaints are first presented to the general practitioner, and it is very heartening to note the keen interest and accurate judgment of many general practitioners in dealing with diseases of the chest. I believe that the recent and future developments in the field of diseases of the chest have greatly complicated the diagnosis and management of such disorders. However, the steadily increasing effectiveness with which thoracic diseases may be treated adds to the interest and sense of satisfaction enjoyed by the attending physician, and contributes materially to the length of life, happiness, and productivity of the patient.

** Abstract of lecture delivered before the New Mexico Clinical Society on January 14, 1949.

Periarteritis Nodosa: A Brief Resume*

Periarteritis nodosa is a disease of vascular origin, characterized by occlusion of the lumen of medium-sized arteries by thrombus, thickening of arterial wall, principally the media; aneurysm formation; and rupture of artery with hemorrhage. As a result of impairment of blood supply, tissues and organs nourished by these arteries are affected with inflammatory and later degenerative changes.

Rich and others have shown that this reaction results as a sensitivity phenomenon. Such sensitivity has been reported following use of sulfonamides, thiouracil, quinine, and aspirin, and could conceivably occur as an allergic response to any drug or bacterial organism.

PROTEAN DISEASE

As arteries anywhere in the body may be involved, the disease is protean in its manifestations. The most common symptoms are referable to the tissues or organs most commonly involved. These symptoms have been adequately outlined previously [1].

Non-specific symptoms and signs, such as weakness, tachycardia, fever, loss of weight, leukocytosis, anemia, and emaciation, are commonly seen. Because of the high incidence of renal involvement, hematuria, albuminuria, edema, hypertension, uremia, and nocturia are frequent. Cardiorespiratory and gastro-intestinal symptoms are less frequent, but are important parts of the course of the disease in some instances.

Of the nervous system symptoms, neuritis is the most common, occurring in over fifty per cent of the cases. Headache, coma, atrophy, sensory involvement, visual disturbances, vertigo, and convulsions occur in decreasing frequency. Eosinophilia, skin changes such as purpura, and palpable nodules are valuable diagnostic findings when present, but they occur in only 36 per cent, 21 per cent, and 14 per cent of the cases, respectively.

CASES CITED

The symptoms of most interest to physicians primarily interested in rheumatism are pain, stiffness, and swelling of joints. Eight of 14 cases of periarteritis nodosa previously reported from the University Hospital, Ann Arbor, Michigan, developed one or more of these symptoms during the course of the disease. Since publication of that series, one other of the 14 cases (case 12) [1] has subsequently developed rheumatoid arthritis but is otherwise getting along nicely now, ten years after the onset of the disease. Thus in this series of cases, 64 per cent developed some evidence of arthritis.

It is of further interest that one patient in this series (case 14) [1] is now feeling well, nine years after the onset of his periarteritis nodosa.

These two cases would indicate that the prognosis in periarteritis nodosa is not always as bad as previously indicated. Many patients with bizarre symptoms and manifestations for a while, probably have mild cases of periarteritis nodosa from which they recover, the disease never having been suspected or proven by biopsy.

By GEORGE M. JONES, JR., M.D., F.A.C.P., Dallas, Texas

1.—Jones, Geo. M.: Periarteritis Nodosa: With Case Reports, Ann. Int. Med., 16: 920-940, May, 1942.

*—Resume of a paper presented to the Texas Rheumatism Association, San Antonio, Texas, May 2, 1949.

From the Department of Medicine, Southwestern Medical College, Dallas, Texas.

Effect of a Hormone of the Adrenal Cortex (17-Hydro-11-Dehydrocorticosterone: Compound E) and of Pituitary Adrenocorticotropic Hormone on Rheumatoid Arthritis

"Compound E has been administered to 14 patients with severe or moderately severe rheumatoid arthritis. In each case improvement in clinical features and in sedimentation rates began to occur within a few days. When administration of the hormone was discontinued, the disease generally relapsed promptly. Essentially similar clinical results accompanied by various biochemical effects were obtained from the administration of the pituitary adreno-corticotropic hormone (ACTH) to two patients . . .

Selection of Patients.—Since the fall of 1948 we have given compound E more or less continuously to 5 rheumatoid patients, and for periods of eight to sixty-one days to 9 other patients; a total of 14 patients. None had mild or moderate disease. All had 'moderately severe' or 'severe' chronic polyarticular rheumatoid arthritis of four and a half months' to five years' duration, not satisfactorily responsive to much previous therapy. Three patients whose disease was of relatively short duration (4.5, 5 and 5 months) were already considered disabled by rapidly progressive arthritis.

"In earlier cases the total dose of Compound E used on the first day was the same (100 mg.) as that used on later days. One hundred milligrams of E acetate is the chemical equivalent of about 89 mg. of Compound E. Because of the slightly higher molecular weight and slower absorbability of the acetate, we administered in later cases 300 mg. of acetate on the first day, and usually 100 mg. daily thereafter . . .

In each of the 14 patients the initial results were as follows: Within a few days there was marked reduction of stiffness of muscles and joints, lessening of articular aching or pain on motion and tenderness, and significant improvement of articular and muscular function . . . The appetite often was rapidly improved . . . Improved strength frequently was noted. Several patients stressed the loss of the 'toxicity' of the disease and experienced a marked sense of well-being . . . In every case, when Compound E or its acetate was employed, sedimentation rates decreased markedly; . . . Most rates became normal within ten to thirty-five days, . . . When serum globulin was increased and albumin-globulin ratios were low or reversed, the use of Compound E, if continued longer than a few days, lowered concentrations of globulin and normalized albumin-globulin ratios.

"It is of course most unfortunate that the currently available amounts of Compound E and of adrenocorticotropic hormone are so small and may remain so for months to come. The production of Compound E by partial synthesis is being expanded; total synthesis may be an eventuality. The supply of adrenocorticotropic hormone, a complex protein, depends on the availability of pituitary glands. Opportunities to enlarge widely the scope of these investigations in the near future appear to depend on improvements in the production of Compound E."—Hench, P.S., Kendall, E.C., Slocumb, C.H., and Polley, H.F., **Proc. Staff Meetings Mayo Clinic** 24:181 (Apr. 13), 1949.

Venous Thrombosis And Pulmonary Embolism

"Up to January 1, 1948, over 2600 patients at the Massachusetts General Hospital have had specific efforts made to prevent or treat thrombosis and embolism. . . . General prophylactic measures only were used in most patients under the age of 30. Specific treatment was indicated in a few of these because of the previous history of phlebitis or the type of lesion present. Therapeutic specific measures were carried out when indications of thrombosis or infarct occurred.

"Four hundred and ninety-six patients between the ages of 40 and 65 were treated prophylactically by small doses of dicumarol postoperatively. None of these died of pulmonary embolism. . . . We believe that anticoagulants cannot be safely used empirically (because of hemorrhagic danger) and that careful laboratory and clinical control is necessary.

"Prophylactic bilateral superficial femoral vein interruption was done on 871 patients whose age, debility or disease indicated that a high per centage of them would be likely to develop thrombosis of the leg veins. Of these, four died subsequently of pulmonary embolism. This was a highly vulnerable group of patients and based on comparative experience there might have been expected 37 deaths from embolism.

"One thousand two hundred and sixty patients were treated by phlebotomy, thrombectomy and femoral vein interruptions after signs or symptoms indicated that thrombosis had occurred. Of these six died of further emboli. . . . In a small per centage of these patients anticoagulants and lumbar sympathetic procaine blocks were also used."—Allen, A. W., Donaldson, G. A., **Bull. New York Acad. Med.** 24:619, 1948.

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"Therapy". Pressure dressings, local thrombin, thromboplastin, calcium, vitamin C, hykinone, oxycel, tannic acid packs, snake venom, intramuscular whole blood, citrated blood transfusions, and direct whole blood transfusions have all been used in an effort to halt bleeding. All appear to have had no effect with the exception of pressure dressings and direct whole blood transfusions. Citrated blood has had no effect in causing cessation of bleeding, but . . . direct blood transfusions appear to have a direct effect on stopping bleeding."—Halliwell, H. L., and Brigham, L., **Ann. Int. Med.** 29:803, 1948.

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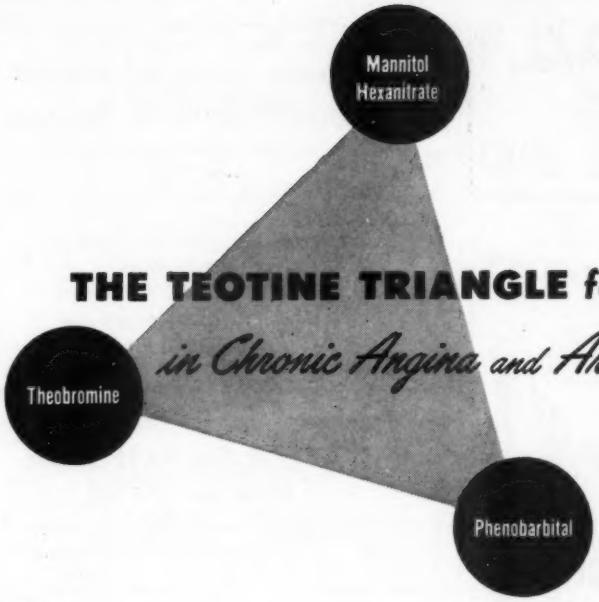

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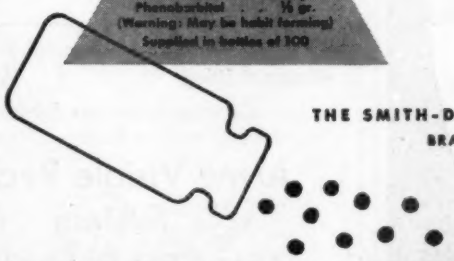

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